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10/527,332	10/26/2005	Ting Liu Carlson	17628.003US1	3516

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EXAMINER	
BADR, HAMID R	
ART UNIT	PAPER NUMBER
1794	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,332	CARLSON ET AL.	
	Examiner	Art Unit	
	HAMID R. BADR	1794	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed on 01/12/2009 is acknowledged.

Claims 29-43 are being considered on the merits.

Claim Rejections – 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 29-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul et al. (US 5,141,858; hereinafter R1) in view of Leathers et al. (US 5,702,942; hereinafter R2).

3. R1 discloses a method for producing oligodextrans for foodstuffs using glucosytransferase of *Leuconostoc mesenteroides (lactic acid bacterium)* strain B-1299. Sucrose is used as the donor molecule and maltose and other sugars as the acceptor molecule. (Abstract and col.2, lines 20 and 26-27).

4. R1 uses maltose as the acceptor molecule. Those of skill in the art know that maltose is a disaccharide composed of two glucose moieties. It is noted that maltose has free hydroxyl groups at positions 2, 3 and 6 which can accept a glucose from sucrose molecule by the action of the enzyme glucosysltransferase. It is also noted that the limitation glucansucrase as presently claimed is a general term for enzymes that can transfer glucose units from sucrose to acceptor molecules such as maltose. They include glucosyltransferases and dextransucrases.

5. R1 teaches that the highest yields of oligodextrans are obtained when the ratio of concentrations of sucrose to the acceptor molecule (e. g. maltose) is between 0.5 and 10. (Col. 3, line 67 – Col. 4, line 3).

6. R1 discloses that after the synthesis of the oligodextran, the fructose (generated from hydrolysis of sucrose) may be kept in the medium or it may be removed by chromatographic ion exchange method methods. (Col. 4, lines 39-41 and col.11, lines 42-44). It is obvious to one of ordinary skill in the art that a low glycemic index sugar substitute should have reduced assimilable sugars such as fructose and glucose.

7. R1 teaches that the oligodextrans produced by the invention are particularly resistant to enzymatic hydrolysis by glucohydrolase enzymes. This property makes them useful as fillers or extenders in sugar substitutes which are metabolizable by man only slightly on not at all (i.e. low glycemic index material). They may therefore be used in low calorie foodstuff formulations (Col. 2, lines 9-21).

8. R1 is silent regarding the alpha-1,3 and alpha-1,6 linkages in the synthesized product. R1 is also silent regarding the specific strain NRRL B-21297.

9. R2 discloses a mutant of *Leuconostoc mesenteroides* that produces a high proportion of alternan to dextran and a high proportion of alternansucrase to dextransucrase (Abstract).

10. R2 discloses that alternan and alternan derivatives have potential value as non-caloric, carbohydrate based soluble food additives in artificially sweetened foods (Col. 1, lines 33-35).

11. R2 teaches that alternans have alpha-1,3 and alpha-1,6 linkages between constituent glucose units (Fig. 1). It is noted that the alpha-1,3 and alpha-1,6 linkages alternate throughout the molecule. It is also noted that the alpha-1,6 linkages can be broken by glucoamylase. Therefore, it is obvious to one of ordinary skill in the art, that the alternan molecule can be processed to have the percentage of alpha-1,3 and alpha-1,6 bonds as presently claimed. Treatment of the final product with glucoamylase is also taught by R1 (see R1 abstract).

12. R2 discloses that one of the mutants of *L. mesenteroides* obtained has been assigned the accession number NRRL B-21297 (Col. 9, lines 53-56). This strain is presently being claimed to be the source of the glucansucrase presently claimed.

13. The process of synthesizing an oligodextran through the use of a glucosyltransferse (glucansucrase) has been clearly disclosed by R1 using strain B-1299 as the enzyme source. R2 on the other hand discloses strain B-21297 as the source of the enzyme and clearly sets forth the advantage of using it to produce more of alternan rather than dextran. It would have been obvious to one of ordinary skill in the at, at the time the invention was made, to follow the teachings of R1 and make a modification of those teachings by replacing the enzyme with the enzyme taught by R2. One would do so to make a different profile of the carbohydrates synthesized. Absent any evidence to contrary and based on the combined teachings of the cited references, there would be a reasonable expectation of success in making low glycemic index carbohydrates.

Response to Arguments

Applicants' arguments have been thoroughly reviewed. These arguments are not deemed persuasive.

1. Applicants argue that the carbohydrates taught by the prior art references do not release glucose into the blood stream and as explained may not be categorized as low-glycemic.

a. By referring to the claimed invention one finds that sucrose is being hydrolyzed by glucansucrase and the resulting glucose is being transferred to an acceptor molecule such as maltose. other technical features of claims 29-33 are the ratios of sucrose to maltose (8:1 to 10:1) and the presence of α, 1-3 and α, 1-6 linkages in the oligosaccharides produced.

In the course of sucrose hydrolysis, fructose is released because sucrose is made of glucose and fructose, the glucose is being transferred to maltose (the acceptor), therefore; fructose will increase in concentration. Claims 34-35 call for removal of this fructose, however, the removal is not complete because claim 35 requires that the sweetener may contain less that 50% fructose. Therefore it may contain 0-49.999% (any value below 50%) fructose.

Claims 36-38 disclose that the source of glucansucrase is *Leuconostoc mesentroids* (lactic acid bacteria) and that that the strains of interest are the designated bacterial strains of Northern Regional Research Laboratories (NRRL) including strains 1297, 1298 and 21297.

Claim 30 limits that the glucansucrase enzyme to *Leuconostoc mesentroids* NRRL B-21297.

In claims 40-43, the sweetener and its applications in foods or beverages are being claimed.

A fair reading of Paul et al. (R1) teaches most of the technical features of the claimed invention. (See rejections under Paul et al.). However, the difference of what is taught by Paul and the presently claimed invention is the specific strain of *Leuconostoc mesentroides*. Paul uses strain NRRL B-1299 while strain B-21297 is presently claimed. Therefore, the glucose transfer from sucrose to maltose, the ratio of sucrose to maltose, the bacterial enzyme and the production of fructose in this donor-acceptor type of reaction are disclosed by Paul.

Furthermore, the reactions catalyzed by glucansucrases may be a simple hydrolysis of sucrose in dilute solutions of sucrose when no other carbohydrate is present, or synthesis of glucan by successive transfer of glucosyl units, or oligosaccharide synthesis by the transfer of the glucosyl unit from sucrose (the donor) to maltose (the acceptor). There are no other reactions known for glucansucrases. Paul is teaching the donor-acceptor type of reaction with a ratio of sucrose to maltose from 0.5-10. The presently claimed invention is claiming a ratio of 8-10. These ranges are clearly over lapping.

The products disclosed by Paul intrinsically contain α-1-3 and α-1-6 linkages. The glucansucrases from *L. mesentroids* NRRL B-1299 (as used by Paul et al.) are known in the art to be produced by the expression of two genes. The glucans produced will have both α,1-3 and α,1-6 linkages. However, Paul talks about α-1-2 linkages to show that certain oligosaccharide structures are branched. Furthermore, the mixture

produced after the enzymatic reaction as disclosed by Paul will contain other simple sugars, and oligosaccharides as well. The argument by the applicants that Paul discloses a product with only α,1-2 linkages can not be substantiated because Paul specifically makes it clear that if is desired to eliminate oligosaccharides which do not contain α, 1-2 glucoside bonds from the reaction mixture, glucoamylase can be used to bring about the total hydrolysis of oligosaccharides which do not contain α, 1-2 linkages. (R1, col. 4, lines 49-56). On the other hand the present claim 1 calls for at least 20% α, 1-3 and at least 20% α, 1-6 linkages. This statement does not mean that there are no α, 1-2 linkages in some of the oligosaccharides produced by the applicants. There is no data in the present specification to show the absence of α, 1-2 linkages in the mixture of carbohydrates produced by applicants either.

The source of the enzyme from the specific strain being claimed (*L. mesenteroides*, NRRL B-21297) is disclosed by Leathers et al. (R2)

However, Leathers does not take advantage of the donor-acceptor type reaction. The carbohydrate substrate is sucrose.

Therefore, since all limitations as presently claimed are met, combined teachings of the references make the presently claimed processes obvious and mixtures of carbohydrates produced according to these processes will be as presently claimed.

2. Applicants argue that the sweetener presently claimed is a full calorie sweetener and the carbohydrates of the cited prior art references are zero calorie additive.

a. The applicants are using the full-calorie sweetener terminology without clarifying the fact that if such sweetener is full-calorie *in vitro* or *in vivo*. It should be realized that

all carbohydrate based materials are full-calorie substances for their nature and all will produce 4 Calories per gram *in vitro*. Therefore from this point of view the carbohydrates disclosed by the cited prior art will be full-calorie materials. However, if such sweetener is full-calorie *in vivo* it should have either α, 1-4 linkages between glucose units exemplified by starch and maltose and oligosaccharides contained in corn syrup and corn syrup solids, or it should be simple sugars such as glucose and fructose or even a sugar like lactose (β, 1-4 linkage). However, claim 1 limits the α-linkages to α, 1-3 and α, 1-6 linkages. Some α, 1-6 linkages can be hydrolyzed by natural human α-glucosidase present in the digestive system when they are accessible in the molecule. That is why starch amylopectin can be assimilated. However, the presence of α,1-3 linkages or the unclaimed α,1-2 linkages causes the product not to be full caloric. The mixture of carbohydrates as disclosed by Paul will also be full caloric (at least *in vitro*).

On the other hand, applicants do not present any data that the sweetener is full caloric *in vivo*. As mentioned above, the *in vitro* calorie content of all carbohydrate based materials are the same and equivalent to 4 Calories per gram of carbohydrate. Further, the α, 1-2 bonds in products disclosed by Paul are indicative of branching points in a portion of oligosaccharides produced. Paul further states that if it is desired to eliminate the oligosaccharides which do not contain an α, 1-2 glucoside bond, from the reaction mixture, the latter may be subjected to the action of hydrolases such as glucoamylase. Then it is clear that oligosaccharides without α, 1-2 bonds are also synthesized and that their hydrolysis by glucoamylase shows they have glycemic index.

The glucansucrases by *L. meenteroides* produce both α, 1-3 and α, 1-6 linkages. Table 2 (Paul, Col. 6 and top of Col. 7) also clearly shows that the reaction mixture contains fructose, maltose, panose (trisacharide), oligodextran of D.P. 4 and of course oligodextrans containing α, 1-2 linkages. The data in Table 2 indicate that based on the type of carbohydrates, the mixture is full caloric too.

Paul further discloses the glucoamylase reaction which generates glucose. Therefore, at least in an *in vitro* procedure, the product as disclosed by Paul has a glycemic index and it is a full calorie carbohydrate *in vitro*.

3. Applicants argue that the products obtained by the combination of Paul and Leathers is not sweet on its own and that the presently claimed product is sweet on its own.

a. Sweetness is a property of sugars and lower molecular weight oligosaccharides. Starting with maltose and sucrose as disclosed by Paul, one ends up with a mixture of fructose, maltose, panose, and oligosaccharides of higher molecular weight as presented in Table 2 (Paul, Cols., 6-7). This mixture is sweet on its own. The applicants are using substrates containing 65-95% maltose. It is obvious that the mixture remaining after the process will contain sugars, low molecular weight oligosaccharides similar to those disclosed by Paul which have a sweet taste.

Furthermore, Leathers disclose that products of enzymes associated with *L. mesenteroides* can be used in artificially sweetened foods. (Col. 1, lines 32-36).

The applicants' argument that the product (one single species amongst the mixture of carbohydrates) containing α, 1-2 linkage as disclosed by Paul does not have a sweet

taste may be true. However, in the reaction as disclosed by Paul, total of products containing α, 1-2 linkages is only 30% of the total mixture (see Table 2 Col. 7 for yield). Combining these products (containing α,1-2 linkages) with all other products which are produced in the course of the enzymatic reactions as disclose by Paul will produce a mixture with sweet taste. Claim 35 of the presently claimed invention also calls for a fructose content of less than 50%. Fructose is almost twice as sweet as sucrose, it is obvious that if you have some fructose in combination with something as tasteless as starch, it will make the mixture sweet.

On the other hand, since fructose can be fully metabolized in human body without giving rise to glucose in blood, a mixture containing fructose as disclosed by Paul and Leathers as well as the present applicants will be sweet and caloric.

Applicants are trying to compare one of the products of the reactions as disclosed by Paul and Leathers, the products containing α,1-2 linkages on their own as pure product, with a mixture of products produced when high maltose corn syrup or corn syrup solids are used as substrates. It is clear that when sucrose and maltose (donor-acceptor) are used in ratios as disclosed by Paul and when the enzyme source as disclosed by Leathers are used in such reactions, the mixture produced will be low glycemic, full caloric and sweet.

4. Applicants also have tried to focus their criticism basically on Paul in an obviousness type rejection where Paul and Leathers are involved.

a. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections

are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HAMID R. BADR whose telephone number is (571)270-3455. The examiner can normally be reached on M-F, 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith Hendricks can be reached on (571) 272-1401. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hamid R Badr
Examiner
Art Unit 1794

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